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The Diagnostic Accuracy of Palpation and Fine-needle Biopsy and an Evaluation of their Combined Use in the Diagnosis of Breast Lesions

Report on a prospective study in 1244 women with symptoms

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In 1244 women with breast symptoms an evaluation by means of palpation was made with respect to diagnosis of malignancy according to a four-grade scale ranging from "definite cancer" to "no cancer." Aspiration biopsy and cytologic examination were then performed in 984 breast lesions. The diagnosis from the cytologic evaluation ranged from benign, through three grades of atypia (slight, moderate, grave) to cancer. A histologic diagnosis was made in 411 cases and in 28% it was cancer. Cancer was found in 92.5% of the patients with a palpatory diagnosis of "definite cancer," and in 50% of those with a palpatory diagnosis of "strong suspicion of cancer." In all patients in whom cancer was diagnosed cytologically, the same diagnosis was made at histology, while 87.5% of those with grave atypia at the cytologic examination were diagnosed histologically as having cancer. A false negative cytologic diagnosis was made in 4% of the cancer cases. With a combination of palpation and cytology, 91% of the cancer cases fell within the groups "definite cancer," "strong suspicion of cancer" (palpation)/"cancer," "grave atypia" (cytology). No patients with cancer were evaluated as "no cancer" (palpation)/"no atypia" (cytology). In this group of 697 patients, however, one cancer was discovered after 7 months. The investigation showed that a thorough palpatory evaluation is a prerequisite for a good result of aspiration biopsy, in particular to meet the risk of a false negative cytologic diagnosis. The cytologic examination revealed cancer in 6 and 12 cases, respectively, when palpation gave no or some suspicion of cancer, and in many cases it was able to eliminate malignancy suspected on palpation. Cytologic atypia indicated cancer in a relatively high per cent, but was also noted in many cases found to be benign histologically.

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The possibilities of reducing the number of "unnecessary" surgical biopsies by using a combination of palpation and cytology is discussed.

DIFFICULTIES are often encountered in the diagnosis of breast tumors. The most essential problem is the decision of whether or not a malignant tumor is present, but differential diagnosis between different benign lesions is also of great importance as regards therapeutic measures.

Palpation is the natural starting point for all breast examinations and in some cases this is diagnostically sufficient in itself. For the diagnosis of non-palpable breast tumors and when palpation is rendered difficult by large nodulated or fibroadenotic breasts, mammography is a valuable addition, and this method has gained increasing application. False positive and false negative findings of breast cancer are common with palpation, and these may also occur with mammography.¹⁹ A reliable cancer diagnosis requires morphologic examination, and for this, biopsy of the tumor for histopathologic evaluation is the most common procedure.

In recent years the value of fine-needle biopsy and cytologic examination has been discussed in several publications.^{4,15,27,29} Results of so-called triple diagnosis (palpation, mammography and cytology) have been reported by Verhaege et al.²⁶ and Kreuzer et al.¹⁰

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Fine-needle biopsy is a simple method. With an adequate technique a false positive cancer diagnosis is hardly likely.²⁹ A few false negative diagnoses in cancer is unavoidable, however. With a careful technique and with increasing experience the frequency of false negative findings can certainly be reduced.⁴

Since 1967 fine-needle biopsy of breast tumors has been performed routinely at the Department of Clinical Cytology, University Hospital, Uppsala. There is strong evidence that close collaboration between clinicians and cytologists is necessary for optimal use of this method, and evidence has also been obtained that a careful palpatory evaluation is an absolute prerequisite for reduction of the risks of false negative cytologic findings.

We therefore performed a thorough clinico-palpatory examination on a prospective series of totally 1244 women with breast symptoms, and followed this by aspiration biopsy with cytologic examination in about 70% of these patients. The accuracy of the diagnosis by each of the methods and by the combination of the two was evaluated by comparison with histopathologic findings and/or results of followup examination.

Materials and Methods

This prospective series comprised 1244 women who sought medical advice at the University Hospital, Uppsala, for some form of breast symptom during the period August 1972 to October 1973. For the purpose of the investigation a special breast tumor clinic was set up at the Department of Surgery.

All women underwent clinical examination by the same surgeon. Fine-needle biopsy and cytologic examination were performed by three cytologists at the Department of Clinical Cytology. Histopathologic examinations were undertaken by the same pathologist as the Department of Pathology.

The patient's history and the results of palpatory, cytologic and histopathologic examinations were all entered in a special medical record which allowed data analysis of the material. The organization of the activity of the breast tumor clinic has been described separately.⁹

Mammography was also used as a complementary diagnostic method. The results of the mammographic examinations will not be reported here, with the exception of 5 cases where mammography contributed to the diagnosis of occult cancer.

The diagnoses arrived at by palpation, cytology and histology were made independently of one another. After the palpatory examination aspiration biopsy was performed on all well-defined masses. The decision concerning surgical biopsy and histologic examination depended upon both the palpatory and the cytologic findings, special criteria being followed which will be described later. Fig. 1 presents the age distribution of the whole series of patients,

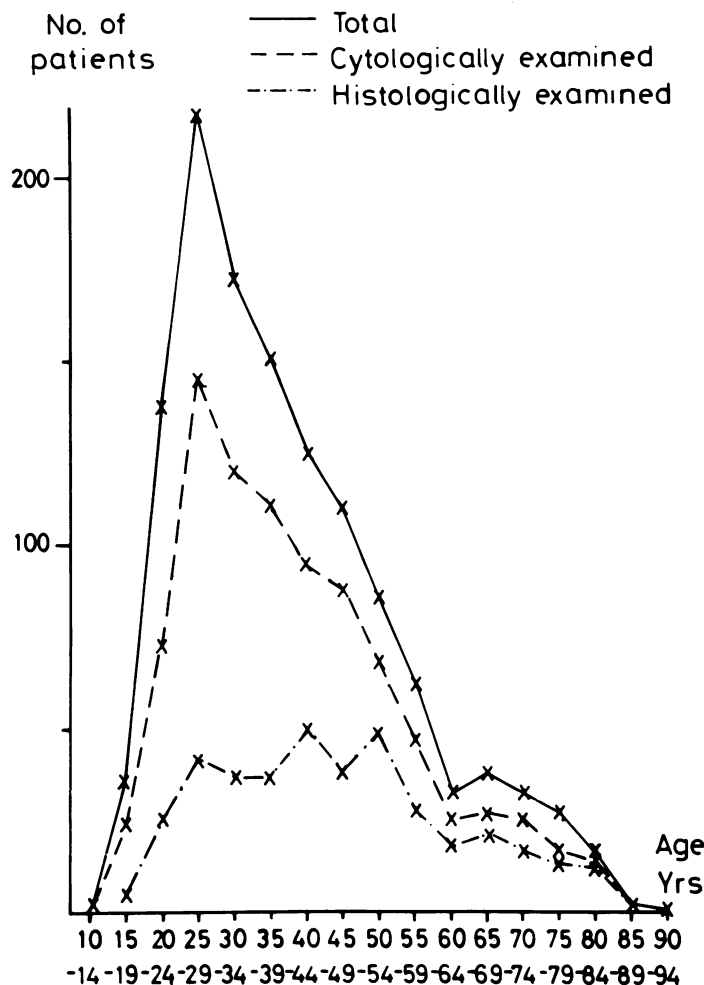


FIG. 1. Age distribution of total material (1244 women) with breast symptoms. Cytologically and histologically examined respectively are also indicated.

of those women who underwent cytologic examination, and of those with a histologic diagnosis.

Clinical Examination with Palpation

The clinical examination included a careful history-taking and inspection and palpation in the sitting or standing and in the supine position. A preliminary diagnosis was made and at the same time a malignancy evaluation was made according to the scale: definite cancer, strong suspicion of cancer, some suspicion of cancer and no cancer. A palpatory diagnosis of "cancer" was given to patients with a malignancy evaluation of "definite cancer" or "strong suspicion of cancer." Other patients were given one of the following diagnoses: normal findings, fibroadenoma, fibroadenosis, solitary cyst, papilloma, lipoma, mastitis or other benign lesion. Fibroadenosis was assessed as localized or diffuse.

When a cytologic examination was planned, the breast was always marked so that there should be no doubt that the

area in question should be examined, and in the cytologic report the position of the lesion or lesions examined was always described.

Cytologic examination

In the aspiration biopsy a modified disposable Franzén instrument described by Hollender and Persson⁷ was used. A needle with a diameter of 0.6 mm was generally used but occasionally slightly coarser needles, though no coarser than 0.8 mm, were employed in order to increase the yield of material. We wish to point out that a repeated palpation of the tumor as well as aspiration biopsy and cytologic examination of the aspirated material (including cyst contents) was always performed by the cytologist.

The clinico-cytologic diagnosis was based upon palpation of the mass and evaluation of its degree of resistance at the aspiration biopsy, combined with microscopic examination of the aspirated cells. In all essentials the cytologic diagnoses were classified according to the same system as in the histopathologic examination (see below). By and large the diagnosis was made in accordance with the criteria previously described by Zajicek.²⁸

In several cases the cells exhibited atypical changes, but not of such a nature or grade as to fulfill the criteria for a diagnosis of cancer. In these cases the cells were irregular in contour and chromatin structure and showed an increase in the nucleo-cytoplasm ratio and in the nuclear staining. The number of cells, the tendency to dissociation and the intercellular variation were also attributed importance in the evaluation. In these cases the described changes were evaluated quantitatively, into slight, moderate and grave atypia.

Histopathologic examination

A conventional histologic technique, with embedding of the material in paraffin was used. In patients in whom the cytologic examination did not give a clear diagnosis of cancer but in whom cancer was strongly suspected on the basis of palpatory and/or cytologic findings, frozen sections were examined. The histologic diagnoses for benign lesions were fibroadenoma, fibroadenosis, papilloma, solitary cyst, lipoma and mastitis. The term fibroadenosis included, in principle, the different groups which according to WHO¹⁷ are classified under the name "mammary dysplasia," as well as the lesion in younger women which often goes under the name mastodynia.^{11,16} The histopathologic classification of the malignant tumors followed that of Ackermann.¹

Course of examination and selection criteria

Subsequent to the clinical examination including palpation, 882 of the total 1244 women underwent aspiration biopsy. In the others, normal conditions or diffuse fibroadenosis was found on palpation.

All women with a well-defined mass were subjected to aspiration biopsy. If this examination revealed cancer, no surgical biopsy was performed before mastectomy but if grave atypia was reported, surgical biopsy was always carried out even if the palpatory finding was "definite cancer."

Surgical biopsy was performed as an outpatient clinic procedure when there was only a lesser degree of malignancy suspicion. The surgical biopsy was almost always done under general anesthesia and the following indications were established:

Surgical biopsy was performed: 1) when malignancy was suspected on palpation ("definite cancer," "strong suspicion of cancer," "some suspicion of cancer") if (a) cytologic examination did not reveal a cyst and microscopic cell examination showed normal conditions, and the palpatory findings became normalized; (b) the cytologic examination did not give reason for reconsideration of the palpatory finding (e.g. fibroadenosis became mastitis); 2) when palpation gave no reason to suspect malignancy *but* (a) cytology revealed atypia; (b) fibroadenoma was present; (c) blood-stained secretion was present; (d) a well-defined "fibroadenotic" mass was present which had been noticed for longer than a few months. The indication for surgical biopsy increased with age and other risk factors.

After excision of a benign lesion a followup was performed about 6 months later, as a rule, when the patient was over 35 years, and on special indications in younger women. The following well-defined groups were checked at intervals: 1) women with any degree of suspicion of malignancy on palpation at the first examination; 2) women exhibiting cytologic atypia; 3) women in whom a solitary cyst had been evacuated.

Also followed up were the majority of women over 40 years of age even if there were no pathologic findings at the first examination. The followup took place after 3-6 months and subsequently as deemed necessary for up to 2 years following the first visit. At the followup examinations mammography was used in over 90% of the women over 40 years. All women were instructed in self-examination and were recommended to do this once a month.

Results

Among a total of 1329 breasts with clinical signs of disease, cytologic examination was done in 984 and histologic in 411. In all but 30 of the breasts the histologic examination was preceded by a cytologic one, performed some day before the operative intervention. In 315 breasts neither cytologic nor histologic examinations were performed.

Palpation

The palpatory evaluation of "definite cancer" was concluded in 53 breasts, "strong suspicion of cancer" in 72,

TABLE 1. *Histology in Relation to Palpatory Evaluation of Malignancy in 411 Breasts.*

Histology	Palpation				Total
	Definite cancer	Strong suspicion of cancer	Some suspicion of cancer	No cancer	
Cancer	49	36	18	11	114
Other malignant tumor			1		1
Atypia	2	2	1	0	5
Benign Lesion	2	27	57	205	291
Total	53	65	77	216	411

“some suspicion of cancer” in 111 and 1093 were evaluated as “no cancer.”

All tumors in the “definite cancer” group underwent histology after palpation and aspiration biopsy, whereas 7 out of 72 in the group “strong suspicion of cancer” and 34 out of 111 in the group “some suspicion of cancer” did not undergo histologic examination primarily. This was because the 7 first mentioned lesions proved to be cysts at aspiration biopsy. Among the 34 last mentioned aspiration biopsy revealed mastitis, cysts or fibroadenosis. In the “no cancer” group (1093 breasts) histologic examination was performed in 20% and cytologic in almost 70%.

In Table 1 the histologic diagnosis is presented in relation to the grade of suspected malignancy on palpation. In the group evaluated on palpation as “definite cancer” there were 4 patients with a non-cancer diagnosis histologically. Two of these, however, showed atypia comparable with pre-malignant lesions, one had mastitis and one showed normal histology.

In the group “strong suspicion of cancer” 36 out of 65 breasts with a histologic diagnosis had cancer. In the group “some suspicion of cancer” the corresponding figure was 18 cancers out of 77 breasts with a histologic diagnosis. In this group an occult cancer in a 77-year-old woman was detected during the followup period. In the group with a palpatory evaluation of “no cancer,” 11 cancers were discovered among 216 breast tumors for which a primary histologic diagnosis was made.

Among the 562 breasts with lesions evaluated as “no

cancer” and with no histologic diagnosis but examined cytologically the palpatory diagnosis remained unchanged in 507 breasts after cytologic examination and followup. Among the others, cancer was found in one 49-year-old woman at followup 7 months later. Mammography gave a negative result. At histology the tumor measured less than 10 mm in diameter.

The differential diagnosis between a fibroadenoma and a cyst is difficult. Among 52 histologically verified fibroadenomas the palpatory diagnosis was fibroadenoma in 35 cases (67%) but solitary cyst in 8 cases (15%). Among the tumors which on palpation were diagnosed as solitary cysts, the majority came under the final diagnosis of fibroadenosis. Thus the cyst was evacuated at aspiration biopsy but because of residual palpatory findings surgical biopsy was performed and the histologic diagnosis became cystic fibroadenosis. The comparison between the palpatory and histologic diagnosis, of benign changes, with the exceptions mentioned, showed that the palpatory diagnoses usually gave a fair evaluation of the nature of the breast changes.

Table 2 presents the palpatory malignancy evaluation for tumors with a primary histologic diagnosis and/or subjected to cytologic examination and followup. The cancer series included the two cancers discovered at followup. In the group “definite cancer” a false positive cancer diagnosis was made in 7.5% but half of these diagnoses were atypia (pre-malignant lesion). A false negative cancer diagnosis in the group “no cancer” was made in 1.5% while in the group “some suspicion of cancer” 17.1% had a final diagnosis of cancer.

Cytology

Aspiration biopsy was performed on tumors in 984 breasts. In 381 cases the cytologic results were compared with the subsequent histologic findings (Table 3). In 76 tumors cytologically diagnosed as cancer, the histologic examination also revealed cancer. No false positive cancer diagnosis was made. Among 16 breast tumors with a cytologic finding of “grave atypia” (strong suspicion of malignancy), 15 (87.5%) were given histologic diagnoses of cancer and the other two fat necrosis and fibroadenoma, respectively. In 9 (27%) of the 33 breasts in which cytology

TABLE 2. *Overall Results of Palpation in Breast Lesions With Histologic and/or Cytologic Diagnosis*

Final Diagnosis	Palpation				Total
	Definite cancer	Strong suspicion of cancer	Some suspicion of cancer	No cancer	
No. of breasts	53	72	111	778	1014
Cancer (%)	92.5	50.0	17.1	1.5	11.2
Atypia (%)	3.7	2.8	1.8	—	0.6
Benign lesion (%)	3.8	47.2	81.1	98.5	88.2

TABLE 3. *Cytologic Findings in Relation to Histology in All Breasts Examined Both Cytologically and Histologically*

Histology	Cytology					Total
	Cancer	Grave atypia	Moderate atypia	Slight atypia	No atypia	
No. of breasts	76	16	33	26	230	381
No. of cancers	76	14	9	4	4	107
Cancer (%)	100	87.5	27.3	15.4	1.7	28.1
Atypia (%)	—	—	15.2	—	0.4	1.6
Benign lesion (%)	—	12.5	57.5	84.6	97.8	70.3

revealed moderate atypia, the histologic diagnosis was cancer, and histologic atypia was found in a further 5 breasts, including one case of cystosarcoma phyllodes with uncertain malignancy. Out of 26 breasts in which cytologic examination showed slight atypia, the histologic diagnosis was cancer in 4 cases (15%). The group "no atypia" included tumors in which aspiration biopsy gave an unsatisfactory yield and where there was reason to suspect non-representative samples at the cytologic examination. In this group 4 cancers (1.7%) were diagnosed, which corresponds to our cytologic false negative findings.

In Table 4 the primary cytologic result is related to the final diagnosis for all breasts primarily subjected to aspiration biopsy. For the two cancers discovered at followup, however, the cytologic result at the time of discovery of the cancer (moderate atypia and no atypia) was included. The cancer frequency in the whole group with "moderate atypia" was 24% and in the whole group with slight atypia 8.7%. One cancer was added to the group of "no atypia," from the followup examination, and the cancer frequency in this group then became 0.6%.

Up to this point the results of the cytologic examination have only been evaluated as regards malignant versus benign lesions. As concerns benign lesions patients with a histologic diagnosis of fibroadenosis had this same diagnosis cytologically in the majority of the cases. In 25 breasts the cytologic diagnosis was "normal" (indicating unsatisfactory sampling), in 16 cases the cytologic examination revealed a cyst, in 30 cases fibroadenoma and in 5 cases mastitis. This will illustrate the multifaceted picture pre-

sented by many benign breast tumors, with its consequent diagnostic difficulties.

A cytologic diagnosis of a cyst (content 1 ccm or more) was done in 98 breasts. In 85 breasts the few cells in the cyst fluid showed no atypia. In 7 there were epithelial cells showing a slight degree of atypia and in 2 atypia of moderate grade. Of those 9 cases one proved to have a papillary cancer. In three cases the cytology as well as the histopathology revealed cancer. In the four cancer cases the malignant tumors were situated in the cyst wall. Among the 94 other cyst cases all with atypical epithelial cells were biopsied as were 14 without atypia but with remaining lump after fine-needle biopsy. All other were followed up one or several times for 6 months up to 2 years. No cancer was discovered.

Palpation and Cytology

The value of combining palpation with aspiration biopsy and cytologic examination is illustrated in Table 5. Of the 114 cancer cases detected primarily, 7 did not undergo cytologic examination. Of the remaining 107 cancer cases, 76 were diagnosed cytologically as cancer. Three of these had been evaluated on palpation as "no cancer" and 10 as "some suspicion of cancer." Of the breasts presenting grave atypia at cytology, in 3 cases cancer was not suspected on palpation, and in another 3 there was "some suspicion of cancer." Seventy-three per cent of the cancers was included into the palpatory groups "definite cancer" and "strong suspicion of cancer," and 84% into the cytologic groups "cancer" and "grave atypia." When

TABLE 4. *Cytologic Findings versus Final Diagnosis in All Breasts With Primary Cytologic Examination*

Final Diagnosis	Cytology					Total
	Cancer	Grave atypia	Moderate atypia	Slight atypia	No atypia	
No. of breasts	76	16	41	46	807	986
No. of cancers*	76	14	10	4	5	109
Cancer (%)	100	87.5	24.4	8.7	0.6	11.1
Atypia (%)	—	—	12.2	—	0.1	0.6
Benign lesion (%)	—	12.5	63.4	91.3	99.3	88.3

*Included two cancers discovered at followup examination (cytology: moderate atypia, no atypia, respectively)

TABLE 5. *Combinatory Diagnostic Accuracy of Palpation and Cytology. Proportion of Cancer in Relation to Benign Lesions in Groups of Diagnostic Combinations*

Cytology	Palpation				Total
	Definite cancer	Strong suspicion of cancer	Some suspicion of cancer	No. cancer	
Cancer	$\frac{42}{42}$ * 100%	$\frac{21}{21}$ 100%	$\frac{10}{10}$ 100%	$\frac{3}{3}$ 100%	$\frac{76}{76}$ 100%
Grave atypia	$\frac{3}{3}$ 100%	$\frac{5}{5}$ 100%	$\frac{3}{4}$ 75%	$\frac{3}{4}$ 75%	$\frac{14}{16}$ 87.5%
Moderate atypia	—	$\frac{3}{6}$ 50%	$\frac{3}{8}$ 37.5%	$\frac{3}{21}$ 14%	$\frac{9}{35}$ 26%
Slight atypia	—	$\frac{1}{8}$ 12.5%	$\frac{1}{7}$ 14%	$\frac{2}{31}$ 6%	$\frac{4}{46}$ 9%
No atypia	$\frac{1}{3}$ 33%	$\frac{2}{26}$ 8%	$\frac{1}{80}$ 1%	$\frac{0}{697}$ 0%	$\frac{4}{806}$ 0.5%
Total	$\frac{46}{48}$ 96%	$\frac{32}{66}$ 48%	$\frac{18}{109}$ 17%	$\frac{11}{756}$ 1.5%	$\frac{107}{979}$ 11%

*The figure over the line represents the number of cancers.

The figure under the line represents the number of all patients in the group.

these palpatory and cytologic groups were combined, 91% of the cancers were detected. The 10 remaining cancer cases (9%) came from the uncertainty groups "some suspicion of cancer" (palpation) and/or "moderate—slight atypia" (cytology). None of the cancers were found in the group "no cancer" (palpation)/"no atypia" (cytology).

The diagnostic certainty of the combination of palpation and cytology in our series is expressed as risk figures. The percentages represent the probability of cancer in combinations of different grades of cytologic and palpatory suspicion of malignancy. The table illustrates the accentuation of the risk of cancer with increasing suspicion of malignancy on palpation, and the even greater accentuation with increasing grades of atypia; also the finding that a cytologic diagnosis of cancer always meant cancer.

Discussion

The palpatory diagnosis entails considerable uncertainty as regards differentiation between benign and malignant breast tumors. Ackerman¹ stated that a correct palpatory diagnosis of cancer was made in only about 50% and that even experienced examiners made the right diagnosis in only 70% of cancer cases. Leis¹¹ gave a figure of 80% and even one of the most experienced diagnosticians, namely Haagensen,⁵ reported a certain frequency of wrong diagnoses in his personal material.

It is important to discuss separately false positive and false negative findings. With the present demands for microscopic verification of the cancer diagnosis prior to definitive surgery, a false positive palpatory diagnosis hardly implies any risk for the patient. A false negative palpatory diagnosis on the other hand, may mean a fatal delay in the initiation of treatment. Ochsner and Griffith¹³ reported a false positive palpatory diagnosis in 4%, while

Storrs²³ had a figure of 30%. Kreutzer et al.¹⁰ could verify a cancer diagnosis in 45% of their patients in whom the palpatory findings indicated suspected cancer and Venet et al.,²⁵ reported a cancer frequency of 35% among patients in whom the clinical impression was "suspicion of malignancy" or "malignant." In our series, 7.5% of the palpatory diagnoses of "definite cancer" were false positive. In cases "strong suspicion of cancer" on palpation the cancer frequency was 50%, and in those with "some suspicion of cancer" it was about 20%. The cancer frequency rose almost linearly with the suspicion of malignancy in the present series, but a certain frequency of false positive cancer diagnoses on palpation is inevitable.

Frequency figures for false negative cancer diagnosis must always be minimal as very small cancerous tumors are frequently missed at routine histologic examination.¹⁴ The frequency of false negative cancer diagnoses in a biopsy material therefore varies both with the indications for biopsy and with the accuracy of the histopathologic examination, and also, of course, with the criteria for a palpatory diagnosis of "benign lesion." In different materials, false negative cancer diagnosis have been reported in a frequency of 3.6% to just over 20%.^{12,18,23,24,25} In our series when the tumor was examined histologically a false negative palpatory evaluation was made in 5% (Table 1). Among all tumors examined cytologically and evaluated on palpation as "no cancer" the cancer frequency was 1.5% (Table 2).

The method of cytologic examination has long been discussed and Franzén and Zajicek⁴ reviewed the literature on this subject. With the exception of the puncture of cysts, judging from the literature^{5,11} aspiration biopsy has not been used very extensively for the diagnosis of breast tumors. In recent years, however, several series have

been presented in which aspiration biopsy have been employed routinely for this purpose.^{2,4,8,10,15,21}

A prerequisite for the use of cytologic examination as a reliable method is that no false positive cancer diagnoses are made. This demands considerable restriction and stringent criteria for a diagnosis of cancer, which must entail an increase in the number of cases with a diagnosis of strong suspicion of malignancy (grave atypia). No false positive cancer diagnoses were made in the present series. Sporadic case of false positive cancer diagnosis otherwise occur in most of the reported series. The figures varied from a frequency of 5.8%³ to less than 0.1%.⁴

In the present series 107 cancers were examined cytologically. In 71% the cytologic diagnosis was cancer compared with 88-48% in several other series.^{2,4,10,27} Franzén and Zajicek⁴ among others have shown how the reliability in the diagnosis is improved with increasing experience.

When evaluating so-called false positive cytologic cancer diagnoses it is necessary to examine the histopathologic examination just as closely as the cytologic. We have no other frame of reference for the histopathologic examination than an even more thorough macroscopic and microscopic inspection of the specimens. With increased use of mammography more and more small lesions will be discovered which, with a good cytologic technique, will be diagnosable in a large proportion of cases.⁶ Histologic verification of these diagnoses may demand a very thorough scrutiny of the specimens.²²

Stringent criteria for cytologic diagnosis of cancer entail a higher proportion of suspected cancer diagnosis. Evers and Fishedick² made a diagnosis of strongly suspected cancer in 15% of their cancer cases and Zajicek et al.²⁹ in 14%, but Zaidela and Rousseau²⁷ in only 3%. In the present series cytology revealed grave atypia in 14 of the cancer cases (13%) with a high specificity in that only 2 cases diagnosed cytologically as grave atypia were given a benign diagnosis at histology.

Slight or moderate atypia was found in 12% of our cancer cases while Zajicek et al.²⁹ reported atypia in 1.6% and Evers and Fishedick² in 25%. Thus here is an even greater discrepancy between different authors. One of the reasons must be differences in the criteria for a diagnosis of atypia and another the difficulty for even one and the same examiner to apply this criteria strictly.

The reliability of the cytologic examination is entirely dependent upon the representiveness of the aspiration biopsy. False negative findings will therefore be made even in the most thorough examination. The tumor may be missed at the puncture and in tumors with abundant connective tissue it may be difficult to withdraw a sufficiently large number of cells. The frequencies of false negative cancer diagnoses ranged from 7.6% in the series

of Zaidela and Rousseau²⁷ to 26.7% in that of Shiller-Volkova and Agamova.²⁰ In our series a false negative diagnosis was made in 3.7%. As did other authors^{5,11} we found the risk of missing cancers in cyst walls to be minimal.

Our investigation showed that the combination of palpation and cytologic examination gave a high degree of reliability in detecting cancer cases. Ninety-one per cent of the cancer cases were in the groups "definite cancer"—"strong suspicion of cancer" (palpation)/"cancer"—"grave atypia" (cytology) and 9% in the groups "some suspicion of cancer" (palpation)/"atypia" (cytology). In the combination "no cancer"/"no atypia" the risk was 0 and even if we include a later discovered cancer the risk figure was 0.0014 as there were 697 patients in this group. As soon as there was any suspicion of malignancy in the palpatory examination and especially when cytologic atypia was added the probability of cancer rapidly increased.

Haagensen,⁵ among others, has pointed out the importance of restraint in biopsies of "cystic disease." We have shown that under optimal conditions with a combination of palpation and aspiration biopsy good differential diagnosis can be made between various benign changes and we have been able to pick out definite or suspected cancers with a high degree of reliability.

With an active preoperative diagnosis the tumors can be selected such that many surgical biopsies are obviated while the diagnostic certainty nevertheless remains high. Further in many cases where cancer has not been suspected at the palpatory examination a preoperative diagnosis of cancer can be proved.

The advantages of combining palpation and aspiration biopsy can be summarized as follows:

Cytologic diagnosis of cancer obviates preoperative excision. When cancer is suspected at palpation cytology can confirm a diagnosis of cancer (obviates preoperative biopsy), increase the suspicion of malignancy in different varieties of atypia (biopsy necessary), abolish a suspicion of malignancy (cyst), reduce a suspicion of malignancy and possibly obviate an immediate biopsy. When there is no palpatory suspicion of malignancy cytology can give an unexpected diagnosis of cancer, give rise to a suspicion of malignancy (atypia), increase the probability of the palpatory diagnosis "benign lesion" provided a representative sample has been obtained.

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